IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

SEPRACOR, INC., Plaintiff, v. DEY, L.P. and DEY, INC., Defendants.	)	
SEPRACOR, INC., Plaintiff, v. BARR LABORATORIES, INC., Defendant.	)	C.A. No. 06-113-JJF (Consolidated)

DEFENDANTS DEY, L.P. AND DEY, INC.'S
OPENING CLAIM CONSTRUCTION BRIEF

Of Counsel:

Edgar H. Haug
Sam V. Desai
Frommer, Lawrence & Haug LLP
745 Fifth Avenue
New York, NY 10151
(212) 588-0800

Elizabeth A. Leff
Frommer, Lawrence & Haug LLP
1667 K Street, N.W.
Washington, DC 20006
(202) 292-1530

ASHBY & GEDDES
Steven J. Balick (I.D. #2114)
John G. Day (I.D. #2403)
Tiffany Geyer Lydon (I.D. #3950)
500 Delaware Avenue, 8th Floor
P.O. Box 1150
Wilmington, Delaware 19899-1150
(302) 654-1888
sbalick@ashby-geddes.com
jday@ashby-geddes.com
tlydon@ashby-geddes.com

Attorneys for Defendants
Dey, L.P. and Dey, Inc.

Dated: April 10, 2008

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

I. INTRODUCTION

Plaintiff Sepracor, Inc. ("Sepracor") and defendants Dey, Inc. and Dey, L.P. (collectively "Dey") have identified 12 claim terms and/or phrases that require construction. The disputed terms and/or phrases and Dey's proposed constructions are set forth below:

U.S. PATENT NO. 5,362,755

DISPUTED TERMS (CLAIM #)	DEY'S PROPOSED CONSTRUCTIONS
"while reducing side effects associated with chronic administration of racemic albuterol" (claim 1)	Reducing those beta-adrenergic side effects and teratogenic effects associated with the periodic or prophylactic administration of albuterol that are caused directly by the S(+) enantiomer of albuterol.
"while simultaneously reducing undesirable side effects" (claim 1)	At the same time the optically pure R(-) isomer is administered in a quantity sufficient to cause bronchodilation there is a reduction in those beta-adrenergic side effects and teratogenic effects associated with the use of racemic albuterol that are caused directly by the S(+) enantiomer of albuterol.
"chronically administering" (claim 1)	Treating periodically or prophylactically.

U.S. PATENT NO. 5,547,994

DISPUTED TERMS (CLAIM #)	DEY'S PROPOSED CONSTRUCTIONS
"while reducing side effects associated with the acute administration of racemic albuterol" (claim 1)	Reducing those beta-adrenergic side effects and teratogenic effects associated with the administration of racemic albuterol to a patient after the onset of an asthma attack that are caused directly by the S(+) enantiomer of albuterol.
"while simultaneously reducing undesirable side effects" (claim 1)	At the same time the optically pure R(-) isomer is administered in a quantity sufficient to cause bronchodilation there is a reduction in those beta-adrenergic and teratogenic effects associated with the use of racemic albuterol that are caused directly by the S(+) enantiomer of albuterol.

U.S. PATENT NO. 5,760,090

DISPUTED TERMS (CLAIM #)	DEY'S PROPOSED CONSTRUCTIONS
"while reducing side effects associated with the administration of racemic albuterol" (claim 1)	Reducing those beta-adrenergic side effects and teratogenic effects associated with the administration of racemic albuterol that are caused directly by the S(+) enantiomer of albuterol.
"while simultaneously reducing undesirable side effects" (claim 1)	At the same time the optically pure R(-) isomer is administered in a quantity sufficient to cause bronchodilation there is a reduction in those beta-adrenergic and teratogenic effects associated with the use of racemic albuterol that are caused directly by the S(+) enantiomer of albuterol.

U.S. PATENT NO. 5,844,002

DISPUTED TERMS (CLAIM #)	DEY'S PROPOSED CONSTRUCTIONS
"inducing bronchodilation or providing relief of bronchospasm" (claims 1 and 10)	Treating asthma.
"while reducing the concomitant liability of adverse effects associated with racemic albuterol" (claim 10)	Reducing those beta-adrenergic side effects and teratogenic effects associated with the administration of racemic albuterol that are caused directly by the S(+) enantiomer of albuterol.
"while simultaneously reducing said adverse effects" (claim 10)	At the same time the optically pure R(-) isomer is administered in a quantity sufficient to cause bronchodilation there is a reduction in those beta-adrenergic side effects and teratogenic effects associated with the use of racemic albuterol that are caused directly by the S(+) enantiomer of albuterol.

U.S. PATENT NO. 6,083,993

DISPUTED TERMS (CLAIM #)	DEY'S PROPOSED CONSTRUCTIONS
"treating bronchospasm in a patient with reversible obstructive airway disease" (claim 1)	Treating an asthma patient after the onset of an asthma attack (acute treatment).
"preventing bronchospasm in a patient with reversible obstructive airway disease" (claim 10)	Chronically treating a patient for asthma.

As discussed in detail below, Dey's proposed definitions adhere to the well-established principles of claim construction, and therefore this Court should adopt Dey's definitions.

II. NATURE AND STAGE OF THE PROCEEDINGS

Sepracor filed this action for infringement of U.S. Patent Nos. 5,362,755 ("the '755 patent"), 5,547,994 ("the '994 patent"), 5,760,090 ("the '090 patent"), 5,844,002 ("the '002 patent") and 6,083,993 ("the '993 patent) (collectively the "method-of-use patents") against Dey on February 22, 2006. (D.I. 1.) This patent infringement suit is based on Dey's submission to the U.S. Food and Drug Administration ("FDA") of Abbreviated New Drug Application ("ANDA") No. 77-800 seeking approval to market generic versions of three dosage strengths of Sepracor's levalbuterol hydrochloride inhalation solutions. The Sepracor product, sold under the trade name Xopenex®, is approved for the treatment of reversible obstructive airway disease. Ex. 1 at SEP9001815.

On September 27, 2006, Sepracor filed a second suit against Dey based on its filing of ANDA No. 78-309 seeking approval to market a levalbuterol hydrochloride concentrate solution. (D.I. 1 in C.A. No. 06-604 (JJF).) Over Sepracor's objection, the Court granted Dey's motion to consolidate the two actions on December 5, 2006. (D.I. 57.) At issue in the consolidated case is

whether the products described in Dey's ANDAs would, if marketed, infringe any valid or enforceable claim of the method-of-use patents.

Sepracor and Dey have completed fact discovery, and have exchanged opening, rebuttal and supplemental expert reports. Sepracor filed a similar complaint against Barr Pharmaceuticals, Inc. ("Barr") on July 12, 2007. (D.I. 1 in C.A. No. 07-438 (JJF).) Sepracor and Barr are in the midst of fact discovery. On March 20, 2008, this Court consolidated C.A. Nos. 06-113 (consolidated), and 07-438 (JJF) for all purposes. (D.I. 262.) Answering claim construction briefs in this consolidated action are due on May 1, 2008. (D.I. 262.) Thereafter, the parties are to contact the Court to schedule a Markman hearing. (D.I. 262.) A trial date will be set in conjunction with the Court's Markman decision. (D.I. 259 at 31-32.)

III. SUMMARY OF THE ARGUMENT

The claims of a patent serve an important public notice function because they define the boundaries of a patentee's right to exclude. Claim construction begins and ends with the language of the claims. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005). The Court's determination of the meaning of the disputed claim language is assisted by the intrinsic evidence of record including the written descriptions and the prosecution histories. While extrinsic evidence such as dictionaries and treatises may shed light in understanding the meanings of terms and phrases to be construed, the extrinsic evidence plays a limited role and is subordinate to the intrinsic evidence in determining the meaning of disputed claim language. *Id.* at 1317.

In *Phillips* the Federal Circuit stated that "the construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Id.* at 1316 (quoting *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1999) (citations omitted)). As set forth in detail below,

Dey's proposed claim construction provides such an alignment between the claims and the specification and is, therefore, the correct claim construction.

IV. STATEMENT OF FACTS

A. The Development of Albuterol and Levalbuterol for the Treatment of Asthma

Albuterol is a short acting beta$_2$-agonist which has been extensively used to treat asthma since 1969. Albuterol was invented by scientists at Allen & Hanburys (now GlaxoSmithKline plc) who were working to develop a beta-agonist selective for bronchial tissue so as to minimize cardiac effects. Ex. 2 at DLEV500174. In 1966, Allen & Hanburys filed Great Britain Patent Specification No. 1,200,886 ("GB '886") for *inter alia* albuterol and its optically pure isomers.[1] Ex. 2 at DLEV012657. GB '886 discloses how to synthesize racemic albuterol, the use of albuterol and its optically pure isomers as bronchodilators to treat asthma, the symptoms of asthma such as bronchospasm, and various dosage forms and strengths. *See* Ex. 3. Four years later, Allen & Hanburys filed a second patent, Great Britain Specification No. 1,298,494 ("GB '494"). Ex. 4 at DLEV012652-56. GB '494 disclosed a method of synthesizing both of the pure optical isomers of albuterol, identified the R(-) isomer as the therapeutically active isomer and referred the reader to the earlier filed GB '886 patent for a description of "the practical utility" of the isomers. *See* Ex. 4 at DLEV012652, p. 1 ll. 15-22.

B. The Specifications of the Method-of-Use Patents

The method-of-use patents all claim priority to a single parent application, U.S. Patent Application No. 07/461,262 ("the '262 application") filed on January 5, 1990. As a result, they

[1] Albuterol is a 50:50 (racemic) mixture of two isomers R(-) albuterol (levalbuterol) and S(+) albuterol. Isomers are chemically identical and have the same physical properties but are structural mirror images of each other.

share nearly identical specifications.[2] According to the abstract of the specification, the method-of-use patents disclose a method of "utilizing the optically pure R(-) isomer of albuterol for treating asthma . . . ." Ex. 5 at DLEV011524. The background section of the specification identifies albuterol as a drug belonging to the general class of beta-adrenergic compounds. It states that albuterol "acts selectively on $beta_2$-adrenergic receptors to relax smooth muscle tissue, for example, in the bronchial system," and is "most commonly used to treat bronchial spasms associated with asthma . . . ." Ex. 5 at DLEV011525, col. 1 ll. 18-22.

The summary of the invention describes the claimed method as:

> [A] safe, effective method for treating asthma while reducing undesirable side effects, for example, tremor, nervousness, shakiness, dizziness and increased appetite, and particularly cardiac arrhythmia, typically associated with beta-adrenergic drugs. In children, side effects such as excitement, nervousness and hyperkinesia are reduced when the pure isomer is administered. In addition to the above, certain levels of racemic albuterol can cause teratogenic effects, which are believed to be associated with the S(+) isomer. Administering the pure isomer reduces the teratogenic potential which is associated with the S(+) isomer of albuterol.

Ex. 5 at DLEV011525, col. 1 ll. 56-68 (emphasis added). The specification also describes two embodiments of the claimed method: (a) administration after the onset of asthma, and (b) prophylactic administration, which is administration prior to the onset of an asthma attack.

> In the present method, the R(-) isomer of albuterol is administered to an individual who has asthma. For example, R(-) albuterol is administered to an individual after onset of asthma to reduce breathing difficulty resulting from asthma. In another embodiment, optically pure R(-) albuterol is administered prophylactically, that is, before the bronchiospasm begins in an asthma attack, to prevent its occurrence or to reduce the extent to which it occurs.

[2] The only substantive differences between the specifications are the listings of applications to which each patent claims priority. *See* Exs. 5-9.

Ex. 5 at DLEV011525, col. 2 ll. 28-36 (emphasis added). Finally, the specification provides exemplary dosage forms, dosage strengths and modes of administering the R(-) isomer of albuterol. *See e.g.* Ex. 5 at DLEV011525, col. 2 ll. 37-60.

C. Prosecution Histories of the Method-of-Use Patents

The method-of-use patents all derive from the same parent application, U.S. Patent Application No. 07/461,262 ("the '262 application") filed on January 8, 1990. Indeed, Sepracor relied on the prosecution history of the first two patents, the '755 and '994 patents to obtain allowance of the '090, '002 and '993 patents. *See* Ex. 12 at DLEV011756; Ex. 13 at DLEV011658; Ex. 14 at DLEV012406. Only those portions of the prosecution histories of the method-of-use patents relevant to claim construction are discussed below.

1. The Prosecution History of the '755 Patent

The '755 patent, the first of the patents in suit to issue, matured through a series of continuations beginning with the '262 application.[3] Claim 1 of the '262 application, as originally filed, read:

> A method of treating asthma in an individual with albuterol, while reducing side effects associated with albuterol, comprising administering to the individual a quantity of optically pure R(-) isomer of albuterol sufficient to result in bronchodilation, said R isomer being substantially free of its S(+) isomer.

Ex. 10 at DLEV012026. The Examiner rejected all of the claims as obvious in view of the prior art and found that any alleged differences in activity between the R(-) and S(+) isomers of albuterol were not unexpected. Ex. 10 at DLEV012052. Sepracor responded to the Examiner's rejection, stating "[r]acemic mixtures of drugs, including albuterol, suffer from several drawbacks, including side effects associated with one isomer but not the other, and the fact that only one isomer generally has the therapeutic effect." Ex. 10 at DLEV012058. Unpersuaded,

[3] The file histories for the method-of-use patents are found at Exhibits 10-14.

the Examiner issued a Final Office Action on December 9, 1991, rejecting all of the claims. Ex. 10 at DLEV012089-92. The Examiner found that "it has been established that the racemic mixture and isomeric forms of the compounds have been used or tested as bronchodilators in the treatment of asthma." Ex. 10 at DLEV012091.

On June 9, 1992, Sepracor filed a continuation application identified as U.S. Patent Application No. 07/896,725 ("the '725 application") and amended claim 1 to add "while simultaneously reducing undesirable side effects." Claim 1, as amended, read:

> A method of treating asthma in an individual with albuterol, while reducing side effects associated with albuterol, comprising administering to the individual a quantity of optically pure R(-) isomer of albuterol sufficient to result in bronchodilation, while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

Ex. 10 at DLEV012110 (new language underlined). In remarks accompanying this amendment, Sepracor argued that:

> One would be led to assume, from the Examiner's apparent interpretation of In re Adamson et al., that the physiological effects of a racemic compound, both therapeutic and adverse, are elicited by the same isomer. However, this assumption is contrary to Applicants' disclosure which teaches that undesirable side effects are associated with the racemic mixture of the therapeutically inactive isomer, i.e. the S(+) isomer of albuterol, but not with the R(-) isomer. Applicants have, therefore, made the unexpected disclosure that the claimed isomer does not have the same type of activity as the racemic mixture.

Ex. 10 at DLEV012112 (emphasis in original). That is, Sepracor argued that in contrast to what "one would be led to assume"—that both therapeutic and adverse effects were caused by the same isomer—Sepracor unexpectedly found that in albuterol one isomer, the R(-) isomer, was responsible for the therapeutic effects, while the S(+) isomer caused all of the adverse effects.

In an Office Action dated August 10, 1992, the Examiner again rejected all of the pending claims as being unpatentable over the prior art. Ex. 10 at DLEV012116-18. In

response, Sepracor filed a further amendment and submitted a declaration by Dr. Gunnar Aberg ("the Aberg I Declaration"), Vice President of Research and Development, Pharmaceutical Division at Sepracor at the time. Ex. 10 at DLEV012152-57. Sepracor argued that the Aberg I Declaration established that the prior art references did not teach an expectation of decreased side effects as a result of the administration of the optically pure R(-) isomer of albuterol. Ex. 10 at DLEV012124. Sepracor submitted two papers, authored by researchers in the United Kingdom and published after the filing date of the '262 application, arguing that the papers supported Sepracor's claim of reduced side effects. Ex. 10 at DLEV012125. Sepracor also clarified, with respect to the R(-) isomer of albuterol, that the application relates to a reduction in side effects and that "applicant's disclosure does not relate to potency . . . ." Ex. 10 at DLEV012124. In a final Office Action dated June 7, 1993, the Examiner rejected the pending claims over the previously cited prior art for "reasons of record." Ex. 10 at DLEV012205-07.

On July 23, 1993, Sepracor filed an amendment making a clerical change and repeated arguments that had been advanced previously:

> The examiner has suggested that increased potency might be a basis for separating enantiomers. However, to the contrary, and mindful that applicants' disclosure does not relate to potency, the art does not encourage the artisan of ordinary skill to resolve and administer isomers on the basis of potency.

Ex. 10, at DELV012213 (emphasis added). Sepracor also submitted a second declaration of Dr. Aberg ("the Aberg II Declaration") to demonstrate the alleged unexpected results of the claimed methods. Specifically, Dr. Aberg stated that the prior art cited by the Examiner provides no evidence of an advantage of either enantiomer of albuterol on the basis of β_1 versus β_2 specificity. Ex. 10 at DLEV012217. In an Advisory Action dated August 3, 1993, the Examiner rejected all of the claims stating that "the declaration is not persuasive since differences between

isomers, whether regarding increased activity or undesired effects, are not unobvious." Ex. 10 at DLEV012225 (emphasis in original).

On December 7, 1993, Sepracor filed a second continuation application that repeated the arguments previously advanced. Ex. 10 at DLEV12251-62. On February 25, 1994, a new examiner assigned to the file rejected the claims stating "it would have been obvious to the skilled artisan that each isomer would not possess the same efficacy or side-effect profile as the other given that the activity exhibited by the racemate would have been recognized as the result of the additive actions of each isomer." Ex. 10 at DLEV012267. The Examiner concluded the claims were unpatentable over the cited prior art references for reasons of record. Ex. 10 at DLEV12265-73. On May 3, 1994, an examiner interview was held. The Examiner stated in his interview summary that he:

> [A]greed that methods of treating a chronic asthma patient w/R(-) isomer of albuterol would be patentable since data shows that airway hyperactivity is unexpectedly avoided in such patients. However, support for such chronic treatment is questioned in light of the specification. Composition claims would remain rejected.

Ex. 10 at DLEV012274 (emphasis added). Thus, the Examiner would not allow the claims until Sepracor identified in the specification support for the treatment of "chronic" asthma.

On May 12, 1994, in response to the Examiner's rejection, Sepracor amended independent claim 1 limiting the claim to "chronically administering" a sufficient quantity of pure R(-) isomer of albuterol to result in bronchodilation. Amended claim 1 then read:

> 1. A method of treating asthma in an individual with albuterol, while reducing side effects associated with chronic administration of racemic albuterol, comprising chronically administering to the individual a quantity of optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

Ex. 10 at DLEV12275-76 (new language underlined). In response to the Examiner's concern that there was no support in the specification for "chronic administration" and "chronically administering," and in order to obtain allowance of the claims, Sepracor submitted the declaration of T. Scott Johnson M.D. Dr. Johnson stated:

> [T]he concept of chronic administration is implicit in the description of modes of administration that is found in the specification. In particular...the concepts of the two modes of therapy (acute and chronic) are discussed. In the first mode (acute) the albuterol is administered "after onset of asthma". In the second, albuterol is administered "prophylactically, that is, before the bronchiospasm [sic] begins in an asthma attack, to prevent its occurrence . . . To be noted is the distinction between asthma (a condition or disease state) and an asthmatic attack (an acute episode of coughing, wheezing or gasping), which often accompanies the general disease state. Asthmatic attacks can be treated acutely; asthma is treated chronically . . . Thus, although the term "chronic" is not used, its implication is clear in the description of prophylactic therapy. . . . Thus the person of skill in the art would understand that the application was referring to chronic therapy when it speaks of either prophylactic or periodic administration.

Ex. 10 at DLEV012281-82 (emphasis added). Thus, according to the declaration of Dr. Johnson, which Sepracor relied upon to get the claims allowed, the terms prophylactic or periodic administration, both of which are found in the specification, would be understood by one of ordinary skill to refer to chronic treatment. On July 26, 1994, the Examiner mailed a Notice of Allowability. Ex. 10 at DLEV0112291. According to the Examiner's Statement of Reasons for Allowance:

> Applicants' amendment and the declaration of T. Scott Johnson filed May 11, 1994 have been received, entered and favorably considered. The Examiner agrees with the statements made by both applicants and the declarant that support exists in the present specification for avoidance of the side effects associated with chronic therapy for asthma. Moreover, it is the Examiner's opinion that it would not have been expected from the prior art of record that the R(-) isomer of albuterol would possess the improved side effect profile as established in the declaration of Dr.

> Aberg filed July 23, 1993, i.e., that the R(-) isomer of albuterol does not cause the hypersensitivity reaction normally associated with long-term racemic albuterol administration in patients suffering from asthma.

Ex. 10, at DLEV012292-93. The '755 patent issued on November 8, 1994.

2. The Prosecution History of the '994 Patent

U.S. Patent No. 5,547,994 matured from U.S. Application No. 08/335,480 filed on November 7, 1994. That application was a continuation of the applications discussed above which matured into the '755 patent. The claims initially filed were identical to those initially filed in the '262 application. On June 9, 1995, Sepracor amended those claims to "parallel the allowed claims in patent application Serial No. 08/163,581 (Now U.S. Patent 5,362,755); the sole difference is that the claims in the parent related to reducing side effects upon chronic administration and the instant claims relate to reducing side effects associated with acute administration." Ex. 11 at DLEV011907 (emphasis in original). Sepracor argued:

> Support [in the specification] for the amendment is found on page 4, line 4 to line 13. The reference to the administration of albuterol to an individual "after onset of asthma to reduce breathing difficulty" (line 7) reflects acute medication, where as the reference to prophylactic treatment (line 10) relates to chronic therapy.

Ex. 11 at DLEV011907. Sepracor reminded the Examiner that he allowed the '755 application for the use of the R(-) isomer of albuterol to treat asthma while avoiding the side effects associated with chronic administration, but he did not believe that applicants had support to claim a reduction of side effects associated with acute administration of racemic albuterol. Ex. 11 at DLEV011912.

In an attempt to support claims for the reduction of side effects associated with acute administration of racemic albuterol, Sepracor submitted the Declaration of Dean A. Handley ("the Handley Declaration"), who was at the time Sepracor's Associate Director of

Pharmacology. According to the Handley Declaration, racemic albuterol, R(-) and S(+) albuterol each cause tremors upon a single dose. "By removing the S enantiomer, one maintains the bronchodilatory effects of racemic albuterol while providing half the tremorigenic dose." Ex. 11 at DLEV011913. The Examiner was unpersuaded and issued a Final Rejection on September 25, 1995, in view of the previously cited prior art. Ex. 11 at DLEV011933-37.

On November 16, 1995, an examiner interview was held. The Examiner's summary states:

> Reviewed prior art, agreed that differences were present between the isomers but could not agree that differences were unexpected. Applicants are invited to submit a response outlining what was known would have been expected vs. what applicants have found and how these findings support a conclusion of non-obviousness in light of In re Adamson.

Ex. 11 at DLEV011938 (emphasis in original).

In response, Sepracor submitted a Declaration by Dr. McCullough ("the McCullough Declaration"), at the time Sepracor's Senior Director of Pharmacology. The McCullough Declaration presented details of an experiment showing exposure of airway smooth cells to S(+) albuterol increased basal calcium levels while exposure to R(-) albuterol decreased basal calcium levels. Ex. 11 at DLEV011950-58. Dr. McCullough concluded "[t]he changes in calcium handling observed in the experiments . . . represent a potential mechanism for bronchial hyperactivity following acute administration of S-albuterol . . . . " Ex. 11 at DLEV011955.

On April 11, 1996, the Examiner issued a Notice of Allowability. Ex. 11 at DLEV011993. The '994 patent issued on August 20, 1996.

3. The Prosecution History of the '090 Patent

U.S. Patent No. 5,760,090 issued from Patent Application No. 08/691,604 ("the '604 application") which was a continuation of the preceding applications. On August 15, 1996

Sepracor filed the '604 application with claims 1-12. Ex. 12 at DLEV011728-29. In response the Examiner issued an election restriction requirement finding claims 1-8 were drawn to a method for treating asthma while claims 9-12 were drawn to a pharmaceutical composition of R(-) albuterol. Ex. 12 at DLEV011750-52. On May 7, 1997, Sepracor filed a Preliminary Amendment cancelling the original claims and substituting claims numbered 13 through 23. Ex. 12 at DLEV011753-58. Claims 13 through 22 combined the claims issued in the '755 and '994 patent. Sepracor presented new claim 23, which "combines the substance of the claims of the parent (now US patent 5,547,994), which relate to acute medication, with the substance of the claims of the grandparent (now US patent 5,362,755), which relate to chronic medication, eliminating the division between acute and chronic, but making no other change." Ex. 12 at DLEV011757-58.

Independent claim 23 read:

> 23. A method of treating asthma, while reducing side effects associated with the administration of racemic albuterol, comprising administering to an individual suffering from asthma a quantity of optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

Ex. 12 at DLEV011755.

In an Office Action dated August 25, 1997, the Examiner rejected claims 13 through 23. Ex. 12 at DLEV011768-72. The rejection was based upon double-patenting type obviousness citing the '755 and '994 patents. On November 20, 1997, Sepracor cancelled claims 13 and 14 (which claimed acute and chronic treatment respectively) to obviate the double-patenting rejection. They amended claims 15-22 to refer to claim 23 (which claimed asthma treatment without distinguishing between acute or chronic asthma treatment) rather than claims 13-14, and submitted a Terminal Disclaimer to obtain allowance of claims 15-23. Ex. 12 at

DLEV011783-86. On December 17, 1997, the Examiner issued a Notice of Allowability of claims 15-23. Ex. 12 at DLEV011790.

4. The Prosecution History of the '002 Patent

The '002 Patent matured from U.S Patent Application No. 09/063,551 filed on April 21, 1998, which was a continuation of the '604 application described above. On April 21, 1998, Sepracor filed a Preliminary Amendment changing the name of the patent, canceling original claims 1-12 and adding new claims 13-22 claims. Claims 13 and 22 were independent claims. Ex. 13 at DLEV011655-59. Independent claim 13 read:

> 13. A method of inducing bronchodilation or providing relief of bronchospasm, comprising administering to an individual a quantity of optically pure R(-) albuterol sufficient to induce said bronchodilation.

Ex. 13 at DLEV011656. It is important to note that unlike the claims in the other patents discussed above, independent claim 13 has no language relating to a reduction of side effects caused by the administration of racemic albuterol. Independent claim 22 is identical to 13 except that it includes language relating to reduction in adverse effects caused by racemic albuterol. Independent claim 22 reads:

> 22. A method of inducing bronchodilation or providing relief of bronchospasm while reducing the concomitant liability of adverse effects associated with racemic albuterol, comprising administering to an individual a quantity of optically pure R-(-) albuterol sufficient to induce said bronchodilation while simultaneously reducing said adverse effects.

Ex. 13 at DLEV011657-58.

In support of the application, Sepracor stated only that in the '262 application claims were allowed to a "method of treating asthma," and the new claims relate to a method for inducing bronchodilation or providing relief of bronchospasms. Ex. 13 at DLEV011658. Bronchospasm is a symptom of asthma causing constriction of the bronchi and bronchodilation

is an expansion of the bronchi to relieve bronchospasm in those being treated for asthma. Ex. 15 p. 5, ¶ 16. According to Sepracor, support for this new language was "found on page 5, line 5-6, page 3, line 8-9 and elsewhere in the specification." Ex. 13 at DLEV011658. Sepracor filed a terminal disclaimer with the Preliminary Amendment to avoid a double patenting rejection based upon the earlier patents for the treatment of asthma, and stated that the claims were allowable for reasons of record in the '602 application (which matured into the '090 patent discussed above). Ex. 13 at DLEV011660-63. On June 24, 1998, the Examiner mailed a Notice of Allowability. Ex. 13 at DLEV011665. The '002 Patent issued on December 1, 1998.

5. The Prosecution History of the '993 Patent

The '993 patent matured from U.S. Patent Application No. 09/466,107 filed on December 17, 1999, which was a continuation of U.S. patent application 09/200,541[4] which was a continuation of the '551 application described above. Sepracor filed a Preliminary Amendment cancelling claims 1-12 and adding claims 13-29. Ex. 14 at DLEV012402-06. A Terminal Disclaimer was filed with the Preliminary Amendment. Ex. 14 at DLEV0012407-08. Independent claim 13 read:

> 13. A method of treating bronchospasm in a patient with reversible obstructive airway disease, comprising administering to said patient a therapeutically effective amount of optically pure R-(-) albuterol.

Ex. 14 at DLEV012403. Independent claim 22 read:

> 22. A method of preventing bronchospasm in a patient with reversible obstructive airway disease, comprising administering to said patient a therapeutically effective amount of optically pure R-(-) albuterol.

Ex. 14 at DLEV012404.

[4] The '541 application, a continuation of the '551 application, claimed formulations of R(-) albuterol and was abandoned. *See* Exhibit 20.

Sepracor's sole argument for patentability was that the claims were allowable with the Terminal Disclaimer for the reasons of record in the '551 application and the '604 application (claiming a method of treating asthma). Ex. 14 at DLEV012406. On March 1, 2000, the Examiner mailed a Notice of Allowability. Ex. 14 at DLEV012409. The '993 patent issued on June 4, 2000. In light of Sepracor's argument for patentability, it is interesting to note that none of the claims of the '993 patent contain language relating to a reduction of side effects.

V. ARGUMENT

A. Legal Standards for Claim Construction

Patent claims define the invention and delimit a patentee's right to exclude. *Phillips*, 415 F.3d at 1312. A district court construes patent claims as a matter of law to determine their meaning and scope. *Markman v. Westview Instrs., Inc.*, 52 F.3d 967, 976, 980 (Fed. Cir. 1995) (en banc), *aff'd* 517 U.S. 370 (1996); *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1455 (Fed. Cir. 1998) (en banc). A district court should construe claim language to discern the meaning it would have to a person of ordinary skill in the art at the time of the invention. *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004).

Broadly speaking, guidance as to the meaning of claim language comes from two sources: intrinsic evidence and extrinsic evidence. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1581-83 (Fed. Cir. 1996). Intrinsic evidence has two components: the patent (claims and specification) and its prosecution history. *Id.* at 1582. Extrinsic evidence consists of all evidence external to the patent and its prosecution history, such as dictionaries, treatises, inventor testimony, and expert testimony. *Markman*, 52 F.3d at 980.

In *Phillips*, the Federal Circuit, sitting en banc, discussed claim-construction principles in detail and provided guidance for district courts to follow when construing claims. 415 F.3d 1303

(Fed. Cir. 2005). The Court noted that there is no "magic formula" for conducting claim construction and instead identified a hierarchy for the intrinsic and extrinsic evidence used to discern the meaning of claim language. 415 F.3d at 1324. The Federal Circuit stated that "the claims themselves provide substantial guidance . . . ." *Id.* at 1314. Accordingly, a district court should look to the words of the claims themselves to ascertain the scope of the patented invention. *Vitronics*, 90 F.3d at 1582. A court should generally assign claim language the ordinary and customary meaning it would have to a person of ordinary skill in the art at the time of the invention, i.e., as of the effective filing date of the patent application. *Phillips*, 415 F.3d at 1313; *see Housey Pharms., Inc. v. AstraZeneca UK Ltd.*, 366 F.3d 1348, 1352 (Fed. Cir. 2004).

The Federal Circuit advised district courts to "rely heavily on the written description for guidance as to the meaning of the claims." *Phillips*, 415 F.3d at 1317. The Federal Circuit found that the while the prosecution history constitutes intrinsic evidence, it may be "less useful" for claim-construction purposes than the written description because it represents an ongoing negotiation between the Examiner and the applicant. *Id.* According to the *Phillips* Court, extrinsic evidence is "less significant than the intrinsic record for determining 'the legally operative meaning of claim language.'" *Id.* (quoting *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 862 (Fed. Cir. 2004)).

In addition to the words of the claims themselves, claim construction requires examination of the patent's written description. *Phonometrics, Inc. v. N. Telecom Inc.*, 133 F.3d 1459, 1464 (Fed. Cir. 1998). The ordinary meaning of claim language is the meaning it would have to those skilled in the art after reading the entire patent, including the written description. *Phillips*, 415 F.3d at 1313. The "role of the specification is to describe and enable the invention" and, therefore, "the claims cannot be of broader scope than the invention that is set forth in the

specification." *On Demand Machine Corp. v. Ingram Indus., Inc.*, 442 F.3d 1331, 1340 (Fed. Cir. 2006). "The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Phillips*, 415 F.3d 1316 (citing *Renshaw PLC v. Marposs Societa per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998)).

Claim construction also requires consideration of the patent's prosecution history. *Markman*, 52 F.3d at 980. Statements made by the applicant during prosecution in support of patentability may supply evidence of the meaning of disputed claim language. *See E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 1438 (Fed. Cir. 1988).

A district court may consider extrinsic evidence to assist it in understanding scientific principles and the technology at the time of the invention. *See Markman*, 52 F.3d at 980. Because dictionaries and treatises—although categorized as extrinsic evidence—provide insight into the ordinary and customary meaning of claim language, the Federal Circuit noted that they are "often useful" in claim interpretation. *Phillips*, 415 F.3d at 1322. However, a court should not use extrinsic evidence to vary or contradict the meaning of claim language where the meaning can be derived from intrinsic evidence. *Phillips* 413 F.3d at 1322. Finally, "if a claim term appears in more than one claim it should be construed the same in each." *Dayco Prods., Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1371 (Fed. Cir. 2003).

B. Dey's Proposed Claim Constructions Should be Adopted Because they Comport with Well-Established Claim Construction Principles

1. The Disputed Terms of the '755 Patent

All of the terms of the '755 patent, the meaning of which the parties dispute, are found in independent claim 1. Claim 1 of the '755 patent reads:

> A method of treating asthma in an individual with albuterol, while reducing side effects associated with chronic administration of

> racemic albuterol, comprising chronically administering to the individual a quantity of optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

Ex. 5 at DLEV011526, col. 4 ll. 6-13. The parties dispute the construction of the underlined terms. Dey believes the phrase "while reducing side effects associated with chronic administration of racemic albuterol" must be construed to mean reducing those beta-andrenergic side effects, and teratogenic effects associated with the periodic or prophylactic administration of albuterol that are caused directly by the S(+) enantiomer of albuterol. Dey maintains that "while simultaneously reducing undesirable side effects" means at the same time the optically pure R(-) isomer is administered in a quantity sufficient to cause bronchodilation there is a reduction in those beta-adrenergic side effects and teratogenic effects associated with the use of racemic albuterol that are caused directly by the S(+) enantiomer of albuterol. The parties also dispute the meaning of "chronic administration" and "chronically administering." Based upon the intrinsic record, e.g., the specification, Sepracor's arguments during prosecution, and the declarations it submitted to the Patent Office, "chronic administration" and "chronically administering" must be construed to mean prophylactic or periodic treatment.

a. "Side effects" must refer to those β-andrenergic or teratogenic side effects caused by the S(+) enantiomer

The phrase "while reducing side effects associated with the chronic administration of racemic albuterol" should be construed to mean reducing those beta-adrenergic side effects and teratogenic effects resulting from prophylactic or periodic use of racemic albuterol caused directly by the S(+) isomer. This meaning is consistent with both the specification and the prosecution history.

The specification provides:

> In these applications, it is important to have a composition which is a potent broncho-dilator and which does not exhibit the adverse side effects of many beta-adrenergic drugs. A composition containing the pure R(-) isomer of albuterol is particularly useful for this application because this isomer exhibits these desired characteristics. The present method provides a safe, effective method for treating asthma while reducing undesirable side effects, for example, tremor, nervousness, shakiness, dizziness and increased appetites, and particularly, cardiac arrhythmia, typically associated with beta-adrenergic drugs. In children, side effects such as excitement, nervousness and hyperkinesia are reduced when the pure isomer is administered . . . Administering the pure isomer reduces the teratogenic potential which is associated with the S(+) isomer of albuterol.

Ex. 5 at DLEV011525, col. 1 ll. 50-68 (emphasis added). As described in the specification, as of the filing date of the priority application, Sepracor stated that use of the R(-) isomer of albuterol did not cause some or all of the side effects associated with beta-adrenergic drugs. The specification provides examples of beta-adrenergic side effects. The specification tells the person of ordinary skill in the art that optically pure R(-) albuterol "does not exhibit the adverse side effects of many beta-adrenergic drugs." Accordingly, use of optically pure R(-) albuterol will reduce side effects "typically associated with beta-adrenergic drugs" that are directly caused by the S(+) isomer as well as teratogenic effects directly caused by the S(+) isomer. Ex. 5 at DLEV011525, col. 1 ll. 60-61.

This construction is confirmed by the prosecution history. During prosecution of the '755 patent, Sepracor made clear that the S(+) enantiomer caused adverse side effects and that use of the optically pure R(-) albuterol would, therefore, have fewer side effects than the use of racemic albuterol which is a 50:50 mixture of the R(-) and S(+) isomers.

> Applicants' invention clearly distinguishes over the prior art by specifying the R(-) isomer, rather than the racemate or the S(+) isomer, to result in bronchodilation and to reduce undesirable side effects associated with beta-adrenergic drugs.

Ex. 10 at DLEV012082. Thus, as Sepracor explained to the Examiner, removal of the S(+) isomer would result in bronchodilation and reduce beta-adrenergic mediated side effects.

Applicants filed the priority application prior to determining which, if any of the beta-adrenergic side effects were caused by the S(+) isomer and would, therefore, be reduced or eliminated by use of the optically pure R(-) isomer. Ex. 16, Young Dep. 100:9-17, Apr. 13, 2007. In the patent specification Sepracor simply listed examples of the beta-adrenergic side effects identified in the literature caused by racemic albuterol. Ex. 16, Young Dep. 193:7-21. During the prosecution of the '755 patent, Sepracor was unable to show that administration of the R(-) isomer reduces beta-adrenergic side effects. This is because, contrary to the inventors' expectations and as disclosed in the prior art, it is primarily the R(-) enantiomer which causes both the therapeutic and adverse beta-adrenergic effects.

During prosecution, however, Sepracor located two articles describing research done in the United Kingdom after the filing of the priority application ("the Morley and Chapman articles") that allegedly demonstrated that the S(+) isomer caused the side effect of hypersensitivity in the bronchial tissue:

> Applicants' disclosure of removing the S isomer so as to reduce side effects, and claims directed thereto, dating to at least January 1990 are novel and non-obvious -- particularly as evidenced by the subsequent Morley and Chapman publications.

Ex. 10 at DLEV012171. Following the publication of the Morley and Chapman articles, Sepracor adopted the argument that the S(+) isomer caused hypersensitivity and that the claimed invention was not obvious because the reduction in hypersensitivity was unexpected.

> Thus, by eliminating the S-isomer and its undesirable hypersensitization, applicants have found an unexpected benefit to the use of the pure R isomer for the treatment of asthma.

Ex. 10 at DLEV012253.

As Sepracor itself stated however, "[a]pplicants did not specifically disclose airway hyperreactivity as a side effect to be avoided . . ." by administration of optically pure R(-) albuterol. Ex. 10 at DLEV012278. Accordingly, by Sepracor's own admission there is no support in the specification to include hyperreactivity in the definition of side effects claimed in the '755 patent. *See Wang Labs., Inc. v. America Online, Inc.*, 197 F.3d 1377, 1383 (Fed. Cir. 1999) (in order to be covered by the claims that subject matter must be sufficiently described as the applicant's invention to meet the requirements of section 112"). The Court should, therefore, interpret "side effects" to mean the beta-adrenergic and teratogenic caused directly by the S(+) isomer. *Eastman Kodak Co. v. Goodyear Tire & Rubber Co.*, 114 F.3d 1547, 1556 (Fed. Cir. 1997) (a court "seeks to interpret claims to preserve, rather than defeat, their validity") (citing *ASC Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577 (Fed. Cir. 1984).

While Sepracor may argue that the patent was granted based upon the alleged reduction in hyperreactivity, it has admitted that there is no support for it in the specification. There is no support in the specification because hyperreactivity was identified by researchers other than the named inventors, published after the filing of the priority application and therefore, was not known to the inventors at the time they filed the priority application. Any alleged reduction in hyperreactivity therefore, cannot be considered to be part of the disclosed invention because the claim cannot be interpreted to include side effects that were unknown to the inventors at the time of the invention. *Phillips*, 415 F.3d at 1313 ("the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of invention, i.e., as of the effective filing date of the patent application").

Sepracor argued in its claim construction brief in the *Sepracor v. Breath* case that in addition to hyperreactivity, the S(+) isomer causes the adverse side effect of interfering with the

R(-) isomer thereby reducing the potency of the R(-) isomer when the R(-) isomer is administered in the form of a racemic mixture. Neither the prosecution history nor the specification contain any support for Sepracor's theory that the S(+) isomer antagonizes the R(-) isomer and thereby reducing the potency of the R(-) isomer. Indeed, to the contrary, Sepracor repeatedly told the Examiner that "Applicants' disclosure does not relate to potency." Ex. 10 at DLEV012124; DLEV012213. "Side effects" must be interpreted to mean side effects that are caused directly by the S(+) isomer not by the S(+) isomer acting to reduce the potency of the R(-) isomer. In addition, those side effects must be construed to be limited to beta-adrenergic side effects and teratogencity because only these side effects are supported by the specification. *Wang Labs.*, 197 F.3d at 1383.

This claim construction is also supported by the prosecution histories of the related applications. During the prosecution of the patent applications maturing into the '994 patent, Sepracor continued to make the argument that the S(+) isomer caused adverse side effects, and that treatment with optically pure R(-) albuterol would reduce the adverse effects experienced when the racemic mixture is administered.

> There is nothing in the prior art to suggest that adverse effects reside in the S-enantiomer and could be avoided by use of R-albuterol, substantially free of the S-enantiomer.

Ex. 11 at DLEV011948. Sepracor never argued that when administered as an optically pure compound, an individual would experience fewer beta-adrenergic side effects because a lower dose of the optically pure R(-) isomer could be utilized. Therefore, "side effects" must be interpreted to mean side effects that are caused directly by the S(+) isomer and not by the S(+) isomer acting to reduce the potency of the R(-) isomer.

b. "Chronically administering" means treating periodically or prophylactically

The phrases "chronically administering" and "chronic administration" appear in claim 1 of the '755 patent as underlined below:

> A method of treating asthma in an individual with albuterol, while reducing side effects associated with chronic administration of racemic albuterol, comprising chronically administering to the individual a quantity of an optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

Ex. 5 at DLEV011526. The phrases "chronic administration" and "chronically administering" do not appear in the '755 patent specification. They were added by amendment during prosecution based upon the Examiner's statement that "methods of treating a chronic asthma patient" would be patentable but that he was not sure that the specification supported the addition of the terms "chronic administration" and "chronically administering." Ex. 10 at DLEV012274-76. Without support for these phrases in the specification, the Examiner did not believe the claims were patentable. Ex. 10 at DLEV012274. In response to the Examiner's concerns about the lack of support in the specification for the claim amendments, Sepracor submitted the declaration of T. Scott Johnson M.D. who stated:

> [T]he concept of chronic administration is implicit in the description of modes of administration that is found in the specification. In particular, . . . the concepts of the two modes of therapy (acute and chronic) are discussed. In the first mode (acute) the albuterol is administered "after onset of asthma". In the second, albuterol is administered "prophylactically, that is, before the bronchiospasm [sic] begins in an asthma attack, to prevent its occurrence . . . ."
>
> To be noted is the distinction between asthma (a condition or disease state) and an asthmatic attack (an acute episode of coughing, wheezing or gasping), which often accompanies the general disease state. Asthma attacks can be treated acutely; asthma is treated, chronically . . ."

> Thus, although the term "chronic" is not used, its implication is clear in the description of prophylactic therapy. . . . Thus the person of skill in the art would understand that the application was referring to chronic therapy when it speaks of either prophylactic or periodic administration.

Ex. 10 at DLEV012281-82 (emphasis added). Sepracor relied upon Dr. Johnson's Declaration to demonstrate that "chronic administration" and "chronically administering," were supported by the specification and that the claims were therefore patentable because, as used in the patents, chronic treatment is what was meant by the prophylactic or periodic treatment identified in the specification. Dr. Johnson's declaration convinced the Examiner to allow the claims. Ex. 10 at DLEV012292-93. Having successfully urged a position in administrative proceedings before the United States Patent and Trademark Office, Sepracor is estopped from taking a contrary position in this litigation where its interests have changed. *See RF Delaware, Inc. v. Pac. Keystone Techs., Inc.*, 326 F.3d 1255, 1262 (Fed. Cir. 2003). Therefore, the claim terms "chronic administration" and "chronically administering" must be construed to mean prophylactic administration or periodic administration.

In its response to Dey's interrogatory No. 2, Sepracor defined "chronic administration" and "chronically administering" to mean "periodic prophylactic administration of racemic albuterol." Ex. 17, p. 3.[5] It is unclear what "periodic prophylactic administration means because neither the specification nor Dr. Johnson's declaration use the terms "periodic" and "prophylactic" together. Indeed Dr. Johnson states that the specification "was referring to chronic therapy when it speaks of either prophylactic or periodic administration." Ex. 10 at DLEV012282 (emphasis added).

[5] It is uncertain whether Sepracor continues to advocate this definition. This is because counsel for Sepracor has proffered a different meaning for the terms "chronic administration" and "chronically administering" in the *Sepracor v. Breath* case. In that opening claim construction brief, Sepracor argues that "[t]he plain language of the claim term[s] provides for 'chronically administering to the individual,' *i.e.*, administering the drug to a human to prevent or reduce the extent to which bronchiospams occur."

In defining chronic, Sepracor has sought to combine two terms which occur in different portions of the specification. The reason for this is clear. Prophylactic administration for treatment of asthma is identified as a use for the R(-) isomer of albuterol in the prior art Great Britain patent published over twenty years earlier. In an attempt to avoid the Court finding the claim limitation "chronic administration" in the prior art, Sepracor seeks to alter the definition of chronic it advocated and the Examiner based allowance on. A patentee cannot advocate one meaning to get a claim allowed and another meaning during litigation. *RF Delaware, Inc.*, 326 F.3d at 1262. There is no support in either the specification or in Dr. Johnson's Declaration for chronic administration or chronically administering to mean "periodic prophylactic." Accordingly, the claim construction advocated by Sepracor cannot be the proper construction.

2. The Disputed Terms of the '994 Patent

All of the phrases of the '994 patent, the meaning of which the parties dispute, are found in independent claim 1. Claim 1 of the '994 patent reads:

> A method of treating an acute attack of asthma, while reducing side effects associated with the acute administration of racemic albuterol, comprising administering to an individual suffering from an acute attack of asthma a quantity of an optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

Ex. 6 at DLEV011531, col. 4 ll. 4-12. The parties' dispute, with respect to the construction of the phrases of the '994 patent, are similar to those with respect to the '755 patent. The parties dispute how "while reducing side effects associated with the acute administration of racemic albuterol" and "simultaneously reducing undesirable side effects" should be construed and the meaning of the term "acute administration."

The primary difference between the method of claim 1 of the '994 patent and the method of claim 1 of the '755 patent is that the method of claim 1 of the '994 patent is directed towards

treating an "acute attack of asthma" while reducing side effects associated with "the acute administration" of racemic albuterol. The remainder of the phrase should be construed in the same way as in claim 1 of the '755 patent. *See Lifetime Prods. v. GSC Tech. Corp.*, 321 F. Supp. 2d 938, 946 (N.D. Ill. 2004) (construing identical, but disputed, language found in four patents in a consistent manner).

Therefore, the preamble phrase "while reducing side effects associated with the acute administration of racemic albuterol" should be construed similarly to the way Dey has proposed above for the similar language found in the '755 patent. That is, to mean reducing those beta-adrenergic and tetrogeneric side effects associated with acute administration of racemic albuterol (i.e. treatment with racemic albuterol after onset of an asthma attack) that are directly caused by the S(+) enantiomer.

a. "Acute administration" should be interpreted to mean treatment after the onset of an asthma attack

In a manner similar to what occurred during the prosecution of the '755 patent, the words "acute administration of racemic" were not part of the originally filed '262 application, but were added during prosecution by amendment. Ex. 11 at DLEV011906. Likewise, the phrase "acute administration" does not appear in the patent specification. Sepracor argued that support for the "acute administration" language "is found on page 4, line 4 to line 13" of the application. Ex. 11 at DLEV0011907. According to Sepracor, "[t]he reference to the administration of albuterol to an individual 'after onset of asthma to reduce breathing difficulty (line 7) reflects acute medication, whereas the reference to prophylactic treatment (line 10) refers to chronic therapy.'" Ex. 11 at DLEV011907 (emphasis added). Therefore, one of skill in the art would properly understand "acute administration" to mean treatment after onset of an asthma attack for the purpose of reducing bronchospasm (breathing difficulty).

This construction is also supported by the declaration of Dr. Johnson filed in support of allowance of the claims that matured into the '755 patent. In distinguishing acute administration from chronic administration, Dr. Johnson says in acute administration "albuterol is administered 'after onset of asthma.'" Ex. 10 at DLEV012281. He goes on to say that asthma attacks are treated acutely where as the condition of having asthma is treated prophylactically. *See* Ex. 10 at DLEV012281-82.

3. The Disputed Terms of the '090 Patent

All of the phrases of the '090 patent, the meaning of which the parties dispute, are found in independent claim 1. Claim 1 of the '090 patent reads:

> A method of treating asthma, while reducing side effects associated with the administration of racemic albuterol comprising administering to an individual suffering from asthma a quantity of an optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects said R isomer being substantially free of its S(+) isomer.

Ex. 7 at DLEV011535, col. 4 ll. 4-9 (disputed phrases underlined). The parties dispute the meaning of the phrases "while reducing side effects associated with the administration of racemic albuterol" and "while simultaneously reducing undesirable side effects.

a. The disputed terms in the '090 patent should be construed in the same manner as the disputed terms in the '755 patent

For the reasons set forth above in Section (V)(B)(1)(a), the phrase "while reducing side effects associated with the administration of racemic albuterol" should be construed to mean reducing those beta-adrenergic side effects and teratogenic effects associated with the administration of racemic albuterol that are caused directly by the S(+) enantiomer of albuterol. Similarly, "while simultaneously reducing undesirable side effects" should be construed to mean at the same time the optically pure R(-) isomer is administered in a quantity sufficient to cause

bronchodilation there is a reduction in those beta-adrenergic and teratogenic effects associated with the use of racemic albuterol that are caused directly by the S(+) enantiomer of albuterol.

The '090 patent is a continuation of the '994 patent which is a continuation of the '755 patent. *See* Ex. 19. The only difference between the language found in claim 1 of the '090 patent and the language found in claim 1 of the '755 patent and claim 1 of the '994 patent is that claim 1 of the '090 patent does not distinguish between "chronic" or "acute" therapy. During prosecution of the '090 patent, Sepracor clarified this distinction stating that claim 1 of the '090 patent "combines the substance of the claims of the parent (now US patent 5,547,994) which relate to acute medication, with the substance of the claims of the grandparent (now US patent 5,362,755) which relate to chronic medication, eliminating the division between acute and chronic." Ex. 12 at DLEV011757-58. Because the remaining language in the phrase is identical to the claim language found in claim 1 of the '755 patent and claim 1 of the '994 patent, for the reasons discussed above, the proper construction of the phrase "while reducing side effects associated with the administration of racemic albuterol" is reducing those beta-adrenergic side effects and teratogenic effects resulting from use of racemic albuterol caused directly by the S(+) isomer.

4. The Disputed Terms of the '002 Patent

Claims 1 and 10 of the '002 patent read:

> 1. A method of inducing bronchodilation or providing relief or bronchospasm, comprising administering to an individual a quantity of optically pure R-(-) albuterol sufficient to induce said bronchodilation.
>
> 10. A method of inducing bronchodilation or providing relief of bronchospasm while reducing the concomitant liability of adverse effects associated with racemic albuterol, comprising, administering to an individual a quantity of optically pure R(-) albuterol sufficient to induce said bronchodilation while simultaneously reducing said adverse effects.

Ex. 8 at DLEV011539, col. 4 ll. 5-8; 30-36. As indicated by the underlining, in both independent claims 1 and 10, the parties dispute the meaning of "inducing bronchodilation or providing relief from bronchospasm." In independent claim 10, the parties also dispute the meaning of the phrase "concomitant liability of adverse effects associated with racemic albuterol."

a. "Inducing brochodilation or providing relief from bronchospasm" means treating asthma

The phrase "inducing bronchodilation or providing relief from bronchospasm" must be construed to mean treating asthma. Bronchospasm is described in the specification as part of the pathophysiology of asthma. *See e.g.*, Ex. 8 at DLEV011538, col. 2.11.17-18 ("asthma relief (e.g., relief from bronchial spasms, shortness of breath)); Ex. 8 at DLEV011538 col. 1 1. 50 ("reduce bronchial spasms associated with asthma"). Bronchodilation is relaxation of the airway smooth muscle. Ex. 18, p. 195. It is described in the specification as the physiology of what is done to treat asthma. *See* Ex. 8 at DLEV011538, col. 1. 11. 54-56 (In treating asthma "it is important to have a composition which is a potent bronchodilator . . .")

That the phrase "inducing bronchodilation or providing relief from bronchospasm" must be construed as a method of treating asthma is confirmed in the prosecution history of related U.S. Patent Application 09/200,541 ("the '541 application"). The '541 application was a continuation of the '551 application, the application which matured into the '002 patent. *See* Ex. 19. As part of its argument for the patentability of the formulation claims of the '541 application, Sepracor stated that "the claims of the issued patents 5,844,002; 5,760,090; 5,547,994; and 5,362,755 relate to methods for treating asthma." Ex. 20 at DLEV011571. Thus, Sepracor itself has stated, in a related application, that the '002 patent relates to a method of treating asthma. *See RF Delaware, Inc. v. Pac. Keystone Techs., Inc.*, 326 F.3d 1255, 1262 (Fed.

Cir. 2003) (Where a party has successfully urged one position in an administrative or legal proceeding, it is estopped from taking a contrary position in a subsequent proceeding where its interests have changed). Sepracor cannot now argue that the '002 patent does not claim a method of treating asthma. Accordingly, the term "method of inducing bronchodilation or providing relief of bronchospasm" must be interpreted to mean a method of treating asthma.

b. "Adverse effects associated with racemic albuterol" has the same meaning as "side effects associated with racemic albuterol" found in claim 1 of the'755 patent

The phrase "adverse effects associated with racemic albuterol" should be construed in the same way as the phrase "side effects associated with racemic albuterol" because the phrases are used synonymously in the patent. That is, for the same reasons described in Section (V)(B)(1)(a) above, it should be construed to mean those beta-adrenergic and teratogenic side effects associated with administration of racemic albuterol that are caused directly by the S(+) enantiomer of albuterol.

The phrase "concomitant liability" must have its conventional meaning because the inventors of the '002 patent did not define it either expressly or by implication. The Federal Circuit has found that in such instances dictionary definitions are useful to understand the plain and ordinary meaning of words. *Phillips*, 415 F.3d at 1314. Consequently, both Sepracor and Dey have relied on dictionary definitions for the definition of the phrase "concomitant liability" as used in the claim. Ex. 17, p. 12; Ex. 21, p. 17.

Reading the phrase as a whole, the phrase "while reducing the concomitant liability of adverse effects associated with racemic albuterol" should be construed to mean reducing those beta-adrenergic and teratogenic side effects associated with the administration of racemic albuterol that are caused directly by the S(+) enantiomer of albuterol.

5. The Disputed Terms of the '993 Patent

The parties dispute the meaning of the phrases "treating bronchospasm in a patient with reversible obstructive airway disease" and "preventing bronchospasm in a patient with reversible obstructive airway disease." These phrases appear in independent claims 1 and 10 of the '993 patent and respectively:

> 1. A method of treating bronchospasm in a patient with reversible obstructive airway disease, comprising administering to said patient a therapeutically effective amount of optically pure R-(-) albuterol.
>
> 10. A method of preventing bronchospasm in a patient with reversible obstructive airway disease, comprising administering to said patient a therapeutically effective amount of optically pure R-(-) albuterol.

Ex. 9 at DLEV011543, col. 3 l. 48 - col. 4 l. 2; col. 4 l. 24-27 (disputed phrases underlined).

a. "Treating bronchospasm in a patient with reversible obstructive airway disease" means treating a patient after the onset of an asthma attack

The phrase "treating bronchospasm in a patient with reversible airway disease" means treating an asthma patient after the onset of an asthma attack. The term "reversible obstructive airway disease" is not used in the specification or the prosecution history. Indeed, the only argument made in the prosecution history of the '993 patent is that the claims are "allowable with a terminal disclaimer for reasons of record in parent applications 09/063,551 and 08/691,604." Ex. 14 at DLEV012406. The '604 application matured into the '090 patent and claims a method of treating asthma. The '551 application, which matured into the '002 patent, claims a method of treating bronchospasm or causing bronchodilation. As described in Section (V)(B)(4)(a) above, during the prosecution of the related '541 application, Sepracor stated that the '002 patent claims "relate to methods for treating asthma." Ex. 20 at DLEV011571. Since the '993 patent was allowable for the same reasons as both the '002 patent and the '090 patent,

and both of those patents relate to methods of treating asthma, the phrase "reversible obstructive airway disease" must also relate to asthma.

Sepracor cannot broaden meaning of the phrase "reversible obstructive airway disease" to include diseases other than asthma because any such an attempt would be unsupported by the specification. As noted above, the term "reversible obstructive airway disease" is not found in the specification, and the patent specification refers only to methods for treating asthma.

That reversible obstructive airway disease refers to asthma is further confirmed by extrinsic evidence, including, publications around the time the primary application was filed. For example, the Guidelines for the Diagnosis and Management of Asthma an Expert Panel Report of the National Heart, Lung, and Blood Institute published in 1991, described asthma as "airway obstruction that is reversible (but not completely in some patients) either spontaneously or with treatment. . . ." Ex. 22, at SEP0743646. Similarly, the 39th Edition of the Physician's Desk Reference indicates reversible obstructive airway disease is used interchangeably with asthma. Ex. 23, p. 1882. In addition, asthma was described in journal articles of the time as a disease characterized by reversible airway obstruction. Ex. 24, p. 1368. Thus, the extrinsic evidence further supports the view that the term "reversible obstructive airway disease" was understood by those of skill in the art at the time the priority application was filed to be synonymous with asthma.

The specification describes bronchospasm as a symptom of asthma treated with R(-) albuterol. Ex. 9 at DLEV011542, col. 1 l. 53. The specification further describes the administration of albuterol "to an individual after the onset of asthma to reduce breathing difficulty resulting from asthma." It states that "R(-) albuterol is administered to an individual in whom asthma relief (e.g. relief from bronchial spasms, shortness of breath) is desired." Ex. 9 at

DLEV011542, col. 2 ll. 34-36. Therefore, the phrase "treating bronchospasm in a patient with reversible obstructive airway disease" as used in independent claim 1 of the '993 patent must mean treating an asthma patient after the onset of an asthma attack.

b. "Preventing bronchospasm in a patient with reversible obstructive airway disease" means chronically treating a patient for asthma

The term "preventing bronchospasm in a patient with reversible obstructive airway disease" means chronically treating a patient for asthma. Dr. Johnson, whose declaration was submitted by Sepracor in support of the allowability of claims of the '755 patent, states in that declaration that the patent specification (which is substantially the same in the '755 patent as in the '993 patent) discloses "two modes of therapy (acute and chronic.)" Ex. 10 at DLEV012281-82. He goes on to describe chronic therapy as a treatment in which "albuterol is administered 'prophylactically, that is, before bronchiospasm [sic] begins in an asthma attack, to prevent its occurrence.'" Ex. 10 at DLEV012281 (emphasis added). Thus, based on the specification and Dr. Johnson's declaration, the term "preventing bronchospasm" must refer to chronic treatment.

As discussed with respect to claim 1 of the '993 patent, reversible obstructive airway disease must be construed to mean asthma. Therefore, the term "preventing bronchospasm in a patient with reversible obstructive airway disease" as used in independent claim 10 must mean chronically treating a patient for asthma.

VI. CONCLUSION

For the foregoing reasons, Dey respectfully request that the Court enter and order construing the phrases of the method-of-use patents as proposed by Dey.

ASHBY & GEDDES

/s/ Tiffany Geyer Lydon

Steven J. Balick (I.D. #2114)
John G. Day (I.D. #2403)
Tiffany Geyer Lydon (I.D. #3950)
500 Delaware Avenue, 8th Floor
P.O. Box 1150
Wilmington, Delaware 19899-1150
(302) 654-1888
sbalick@ashby-geddes.com
jday@ashby-geddes.com
tlydon@ashby-geddes.com

Attorneys for Defendants
Dey, L.P. and Dey, Inc.

Of Counsel:

Edgar H. Haug
Sam V. Desai
Frommer, Lawrence & Haug LLP
745 Fifth Avenue
New York, NY 10151
(212) 588-0800
ehaug@flhlaw.com
sdesai@flhlaw.com

Elizabeth A. Leff
Frommer, Lawrence & Haug LLP
1667 K Street, N.W.
Washington, DC 20006
(202) 292-1530
eleff@flhlaw.com

Dated: April 10, 2008